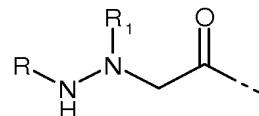


CLAIMS

1. Use of hybrid peptide analogues of peptides or parent proteins, these hybrid peptides containing at least one aza- β^3 aminoacyl residue, namely :

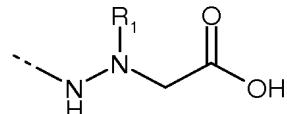
* a residue corresponding to the following formula (A) when it is situated in the N-terminal position,



(A)

wherein R represents H or a protective group of the amine function of the amino acids, such as Fmoc, Boc, or Z, and R1 represents a side-chain selected from those of the amino acids,

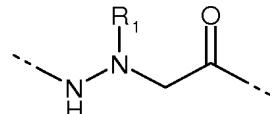
* a residue corresponding to the following formula (B) when it is situated in the C-terminal position,



(B)

wherein R1 represents a side-chain selected from those of the amino acids,

* a residue corresponding to the following formula (C) when it is situated in the chain of the said hybrid peptides,



(C)

wherein R₁ represents a side-chain selected from those of the amino acids, for the preparation:

– of a vaccine or of a medicament intended for the prevention or for the treatment of pathologies associated with the presence, in the body of an individual, of an exogenous or endogenous protein capable of being directly or indirectly involved in the process of appearance and/or development of these pathologies, or

– of a vaccine or of a medicament intended for the prevention or for the treatment of pathologies involving the molecules of the major histocompatibility complex and/or the T cell receptors,

– of a vaccine or of a medicament intended for the prevention or for the treatment of pathologies associated with the presence in the body of an individual of an antibody capable of being recognised by an aforesaid hybrid peptide,

or for the implementation of a method for *in vitro* diagnosis of the aforesaid pathologies.

2. Use according to claim 1, for the preparation of a vaccine or a medicament intended for the prevention or for the treatment of pathologies of viral or bacterial origin, or of autoimmune pathologies, or of neurodegenerative diseases.

3. Use according to claim 1 or 2, for the preparation of a vaccine or a medicament intended for the prevention or for the treatment of the following pathologies:

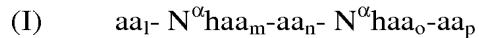
- pathologies involving molecules of the major histocompatibility complex and/or the T cell receptors,
- autoimmune diseases, and in particular Hashimoto thyroiditis, Basedow's disease, Addison's disease, pituitary insufficiency, Biermer's gastritis, certain forms of sterility, type 1 juvenile diabetes, Goodpasture's syndrome, myasthenia, acute articular rheumatism, pemphigus, bullous pemphigoid, herpetiform dermatitis,

vitiligo, alopecia, psoriasis, sympathetic ophthalmia, uveitis, Guillain-Baré's syndrome, multiple sclerosis, haemolytic anaemia, idiopathic thrombocytopenic purpura, idiopathic leucopaenia, primary biliary cirrhosis, active chronic hepatitis, ulcerative colitis, Crohn's ileitis, Gougerot-Sjögren syndrome, rheumatoid polyarthritis, dermatopolymyositis, scleroderma, mixed connective tissue disease, discoid lupus erythematosus and systemic lupus erythematosus.

- neurodegenerative diseases,
- diseases of viral origin, in particular:
 - AIDS caused by human immunodeficiency virus HIV-1 and HIV-2,
 - paraplegia associated with HTLV-1, or adult T cell leukaemia, caused by human T cell leukaemia virus (HTLV virus),
 - infections caused by the syncytial respiratory virus,
 - infections caused by the Coxsackie virus, for example acute lymphocytic meningitis,
 - infections caused by the Epstein-Barr virus, for example infectious mononucleosis,
 - infections caused by the cytomegalovirus, for example cytomegalic inclusion disease,
 - herpes caused by the human herpes virus,
 - herpes caused by herpes simplex virus 6,
 - infections caused by the human parvovirus B19, for example infectious gastroenteritis,
 - hepatitis B caused by the hepatitis B virus,
 - hepatitis C caused by the hepatitis C virus,
 - influenza caused by the influenza virus,
 - rubella caused by the rubella virus,
 - infections caused by the Dengue virus, for example the arboviroses,
 - colds, rhinitis and coryza caused by the rhinoviruses,
 - aphthous fever caused by aphthous fever virus,

- certain cancers linked with viruses, such as the papilloma viruses.

4. Use according to one of claims 1 to 3, of hybrid peptides of the following formula (I) :



wherein :

- aa_l , aa_n and aa_p represent an aminoacyl residue, or a concatenation of aminoacyl residues, corresponding to the aminoacyl residues present at the same positions in the peptide or the parent protein from which the hybrid peptides are derived,

- $N^{\alpha}haa_m$ and $N^{\alpha}haa_o$ represent an aza- β^3 aminoacyl monomer residue, or a concatenation of aza- β^3 aminoacyl monomer residues analogous to the aminoacyl residues initially present at the same position in the peptide or the parent protein from which the hybrid peptides are derived, the said aza- β^3 aminoacyl monomers corresponding to the formulae (A), (B), or (C) shown in claim 1, depending on whether they are respectively in the N-terminal or C-terminal position, or in the chain of the said hybrid peptides, and wherein R_1 is identical to the side-chain of the initial amino acid of the peptide or of the parent protein to which the said aza- β^3 aminoacyl monomers correspond,

- l, m, n, o, and p represent zero, or a whole number lying between 1 and 20, provided that at least one of m or o is different from zero, and that the minimum number of residues in the said hybrid peptides of formula (I) is 4.

5. Use according to one of claims 1 to 4, of hybrid peptides derived from the epitope 88-99 of the histone H4 as parent peptide, and corresponding to SEQ ID NO : 1, at least one of whose initial amino acids is replaced by an aza- β^3 amino acid analogue residue, for the preparation of a medicament, or vaccine, intended for the prevention or for the treatment of systemic lupus erythematosus.

6. Use according to claim 5, of hybrid peptides of the following formulae:

- SEQ ID NO : 2 (or peptide E) :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 3 (or peptide C) :

⁸⁸H₂N-Tyr-Ala-N^α-hLeu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 4 (or peptide A) :

⁸⁸H₂N-Tyr-N^α-hAla-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 5 (or peptide B) :

⁸⁸H₂N-Tyr-N^α-hAla-N^α-hLeu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 6 (or peptide D) :

⁸⁸H₂N-Tyr-Ala-Leu-N^α-hLys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 7 (**or peptide G**) :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-N^α-hTyr-Gly-OH⁹⁹

– SEQ ID NO : 8 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-N^α-hGly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 9 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-N^α-hArg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 10 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-N^α-hArg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 11 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-N^α-hTyr-Gly-OH⁹⁹

– SEQ ID NO : 12 :

⁸⁸H₂N-N^α-hTyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 13 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-N^α-hGly-OH⁹⁹

– SEQ ID NO : 14 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-N^α-hTyr-N^α-hGly-OH⁹⁹

7. Use according to claim 5 or 6, of the hybrid peptide of formula SEQ ID NO : 2, or of the hybrid peptide of formula SEQ ID NO : 7.

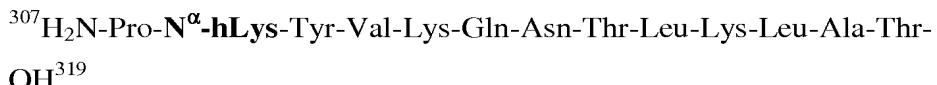
8. Use according to one of claims 1 to 4, of hybrid peptides derived from the peptide 307-319 of the haemagglutinin of the influenza virus as parent peptide, and corresponding to SEQ ID NO : 15, at least one of whose initial amino acids is replaced by an aza- β^3 amino acid analogue residue, for the preparation of a medicament, or vaccine, intended for the prevention or for the treatment of influenza or of any other pathology for which a molecule containing a B or CTL (CD8) epitope is administered in combination with the sequence 307-319 HA which contains a so-called universal T CD4 epitope.

9. Use according to claim 8, of hybrid peptides of the following formulae:

– SEQ ID NO : 16 (or peptide A') :



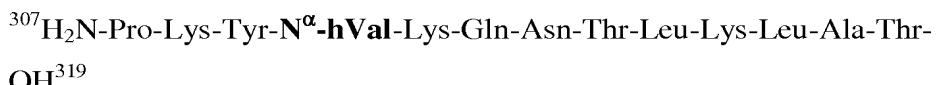
– SEQ ID NO : 17 (or peptide B') :



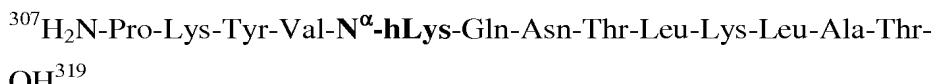
– SEQ ID NO : 18 (or peptide C') :



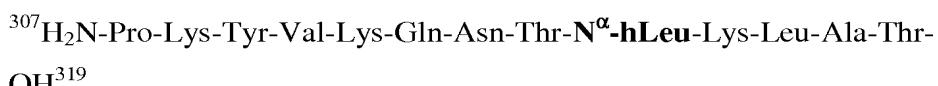
– SEQ ID NO : 19 (or peptide D') :



– SEQ ID NO : 20 (or peptide E') :



– SEQ ID NO : 21 (or peptide F') :



– SEQ ID NO : 22 (or peptide G') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-N^α-hLys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 23 (or peptide H') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-N^α-hAsn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 24 (or peptide I') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-N^α-hLeu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 25 (or peptide J') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-N^α-hAla-Thr-OH³¹⁹

– SEQ ID NO : 26 (or peptide K') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-N^α-hLys-N^α-hLeu-N^α-hAla-Thr-OH³¹⁹

– SEQ ID NO : 27 (or peptide L') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-N^α-hLeu-N^α-hAla-Thr-OH³¹⁹

10. Use according to claim 8 or 9, of the hybrid peptide of formula SEQ ID NO : 25.

11. Hybrid peptides containing at least one aza-β³ amino acid, these hybrid peptides being analogues of peptides or parent proteins, the said hybrid peptides containing at least one initial amino acid of the peptide or of the parent protein.

12. Hybrid peptides according to claim 11, of the following formula (I):



wherein :

– aa_l, aa_n and aa_p represent an aminoacyl residue, or a concatenation of aminoacyl residues, corresponding to the aminoacyl residues present at the same

positions in the peptide or the parent protein from which the hybrid peptides are derived,

- $N^{\alpha}haa_m$ and $N^{\alpha}haa_o$ represent an aza- β^3 aminoacyl monomer residue, or a concatenation of aza- β^3 aminoacyl monomer residues, analogous to the aminoacyl residues initially present at the same position in the peptide or the parent protein from which the hybrid peptides are derived, the said aza- β^3 aminoacyl monomers corresponding to the formulae (A), (B), or (C) indicated in claim 1, depending on whether they are respectively in the N-terminal or C-terminal position, or in the chain of the said hybrid peptides, and wherein R_1 is identical to the side-chain of the initial amino acid of the peptide or of the parent protein to which the said aza- β^3 aminoacyl monomers correspond,
- 1, m, n, o and p represent zero, or a whole number lying between 1 and 20, provided that one at least of m or o is different from zero, that the minimum number of residues in the said hybrid peptides of formula (I) is 4, and one at least of l, n, or p is different from zero.

13. Hybrid peptides according to claim 11 or 12, of the following formulae :

- SEQ ID NO : 2 (or peptide E) :



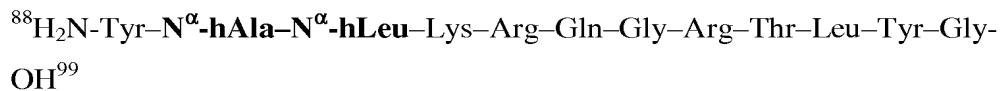
- SEQ ID NO : 3 (or peptide C) :



- SEQ ID NO : 4 (or peptide A) :



- SEQ ID NO : 5 (or peptide B) :



- SEQ ID NO : 6 (or peptide D) :



- SEQ ID NO : 7 (**or peptide G**) :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-N^α-hTyr-Gly-OH⁹⁹

– SEQ ID NO : 8 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-N^α-hGly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 9 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-N^α-hArg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 10 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-N^α-hArg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 11 :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-N^α-hTyr-Gly-OH⁹⁹

– SEQ ID NO : 12 (or peptide F):

⁸⁸H₂N-N^α-hTyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 13 (or peptide H):

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-N^α-hGly-OH⁹⁹

– SEQ ID NO : 14 (or peptide I):

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-N^α-hTyr-N^α-hGly-OH⁹⁹

– SEQ ID NO : 16 (or peptide A') :

³⁰⁷H₂N-N^α-hPro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 17 (or peptide B') :

³⁰⁷H₂N-Pro-N^α-hLys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 18 (or peptide C') :

³⁰⁷H₂N-Pro-Lys-N^α-hTyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 19 (or peptide D') :

³⁰⁷H₂N-Pro-Lys-Tyr-N^α-hVal-Lys-Gln-Asn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 20 (or peptide E') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-N^α-**hLys**-Gln-Asn-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 21 (or peptide F') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-N^α-**hLeu**-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 22 (or peptide G') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-N^α-**hLys**-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 23 (or peptide H') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-N^α-**hAsn**-Thr-Leu-Lys-Leu-Ala-Thr-OH³¹⁹

– SEQ ID NO : 24 (or peptide I') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-N^α-**hLeu**-Ala-Thr-OH³¹⁹

– SEQ ID NO : 25 (or peptide J') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-N^α-**hAla**-Thr-OH³¹⁹

– SEQ ID NO : 26 (or peptide K') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-N^α-**hLys**-N^α-**hLeu**-N^α-**hAla**-Thr-OH³¹⁹

– SEQ ID NO : 27 (or peptide L') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-N^α-**hLeu**-N^α-**hAla**-Thr-OH³¹⁹

14. Hybrid peptides according to one of claims 11 to 13, of the following formulae:

– SEQ ID NO : 2 (or peptide E) :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-**hLeu**-Tyr-Gly-OH⁹⁹

– SEQ ID NO : 7 (or peptide G) :

⁸⁸H₂N-Tyr-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-N^α-hLeu-N^α-hTyr-Gly-OH⁹⁹

– SEQ ID NO : 25 (or peptide J') :

³⁰⁷H₂N-Pro-Lys-Tyr-Val-Lys-Gln-Asn-Thr-Leu-Lys-Leu-N^α-hAla-Thr-OH³¹⁹

15. Polyclonal or monoclonal anti-hybrid peptide antibodies such as are obtained by immunisation of an animal with at least one hybrid peptide defined in one of claims 1 to 14, the said antibodies being capable of forming a complex with these hybrid peptides, and/or with the peptides or parent proteins corresponding to these latter, and characterised in that they recognise the parent peptide or the parent protein with an affinity at least equal to that displayed by the anti-parent peptide or anti-parent protein antibodies towards the parent peptide or the parent protein.

16. Anti-idiotype antibodies capable of forming a complex with the antibodies according to claim 15, such as are obtained by immunisation of an animal with the said antibodies according to claim 15.

17. Complex between a hybrid peptide such as defined in one of claims 1 to 14, and an element of the major histocompatibility complex (also referred to as MHC-complex-hybrid), and possibly a T cell receptor (also referred to as MHC complex-hybrid-T receptor).

18. Complex between a hybrid peptide such as defined in one of claims 1 to 14, and a T cell receptor.

19. Method for *in vitro* diagnosis of pathologies associated with the presence in the body of a patient, of an exogenous or endogenous protein, capable of being directly or indirectly involved in the process of appearance and/or development of these pathologies, characterised in that it comprises:

– contacting a biological sample deriving from a patient capable of being a carrier of antibodies directed against the said protein, with a hybrid peptide such as defined in one of claims 1 to 14, the said hybrid peptide being derived from all or part of the said endogenous or exogenous protein, or derived from a peptide capable of being recognised by antibodies themselves recognising the exogenous or endogenous protein,

under conditions allowing the reaction between the antibodies directed against the protein and capable of being present in the biological sample, and the aforesaid hybrid peptide,

- the *in vitro* detection of the antigen / antibody complex capable of being formed in the preceding stage or
- the *in vitro* detection of antibodies circulating in the patient by a competitive test using an anti-hybrid antibody.

20. Method for *in vitro* diagnosis of pathologies associated with the presence in the body of a patient of an exogenous or endogenous protein capable of being directly or indirectly involved in the process of appearance or development of these pathologies, the said method being characterised in that it comprises:

– contacting a biological sample deriving from a patient capable of being a carrier of the said protein with one or more of the antibodies according to claim 15, the antibodies being advantageously directed against a hybrid peptide derived from all or part of the said endogenous or exogenous protein, or

under conditions allowing the reaction between the protein capable of being present in the biological sample, and the said antibodies directed against the aforesaid hybrid peptide;

- the *in vitro* detection of the antigen / antibody complex capable of being formed in the preceding stage, or
- the detection of antigens circulating in the patient in competitive tests using a hybrid peptide such as defined in one of claims 1 to 14.

21. Outfit or kit for the implementation of the *in vitro* diagnostic methods according to claim 19 or 20, comprising:

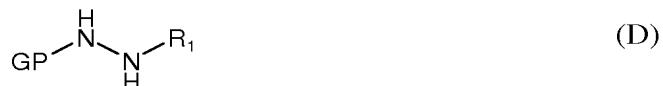
- a hybrid peptide derived from all or part of the endogenous or exogenous protein, or corresponding to a peptide capable of being recognised by antibodies themselves recognising the exogenous or endogenous protein, or else antibodies according to claim 15, directed against this hybrid peptide;
- reagents to render a medium suitable for the formation of an immunological reaction;
- reagents making it possible to detect the antigen / antibody complex which has been formed as a result of the immunological reaction, the said reagents possibly containing a marker or being capable of being recognised in their turn by a labelled reagent, more particularly in the case where the hybrid peptide or the aforesaid anti-hybrid antibodies are not labelled.

22. Pharmaceutical composition, in particular vaccine, characterised in that it comprises a hybrid peptide such as defined in one of claims 1 to 14, or an anti-idiotype antibody according to claim 16, whether or not in combination with a physiologically acceptable vehicle.

23. Pharmaceutical composition characterised in that it comprises a hybrid peptide such as defined in one of claims 1 to 14, or an anti-idiotype antibody according to claim 16, combined with a carrier molecule, whether or not proteic, capable of inducing *in vivo* the production of antibodies neutralising the exogenous or endogenous protein responsible for the pathology, or inducing *in vivo* a cytotoxic or helper cellular immune response.

24. Pharmaceutical composition, characterised in that it comprises antibodies according to claim 15, in combination with a physiologically acceptable vehicle.

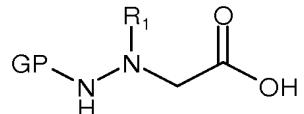
25. Process for preparation of aza- β^3 amino acids characterised in that it comprises a stage of treatment of the substituted and protected hydrazine of the following formula (D) :



wherein R_1 represents a side-chain selected from those of the amino acids, if necessary protected, and GP a protective group of amine functions, such as Boc, Fmoc, or Z,

with glyoxylic acid with stirring in the presence of NaBH_3CN in an acidic medium,

which leads in one stage to the aza- β^3 amino acid compound of formula



wherein R_1 and GP are as defined above, and the said compound can if necessary be deprotected, in particular by means of HCl , of piperidine, or of palladiated hydrogen, in order to remove the group GP and replace it with H.

26. Aza- β^3 amino acids of the following formulae ;

Fmoc aza- β^3 -Glycine (Fmoc- $\text{N}^\alpha\text{hGly-OH}$),

Fmoc aza- β^3 -Lysine (Fmoc- $\text{N}^\alpha\text{hLys(Boc)-OH}$),

Fmoc -aza- β^3 -Aspartic acid (Fmoc- $\text{N}^\alpha\text{hAsp(OtBu)-OH}$),

Fmoc aza- β^3 -Methionine (Fmoc- $\text{N}^\alpha\text{hMet-OH}$),

Fmoc aza- β^3 Arginine (Fmoc- $\text{N}^\alpha\text{hArg (Boc)-OH}$),

Fmoc aza- β^3 -Tyrosine (Fmoc- $\text{N}^\alpha\text{hTyr(OCH}_2\text{OEt)-OH}$),

Fmoc aza- β^3 Asparagine (Fmoc- $\text{N}^\alpha\text{hAsn (Trt)-OH}$),

Fmoc aza- β^3 Proline (Fmoc- $\text{N}^\alpha\text{hPro-OH}$).